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10/587,804	06/07/2007	Thomas Bouquin	0279us310	6931

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,804	BOUQUIN, THOMAS	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6,15,58 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6,15,58 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III, claim 3, in the reply filed on 11/9/2009 is acknowledged.

Applicants state that by way of the present amendments, claims 4-6, 15, and 54-55 depend directly or indirectly from elected claim 3, and newly-added claims 58-65 also depend directly or indirectly from elected claim 3.

Claims 3, 4-6, 15, 54-55, and 58-65 read on Group III.

Applicants' further election of the species of G-418 as the species of aminoglycoside antibiotic in the reply filed on 7/21/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants state that claims 3, 4 and 63 are generic.

Claims 54-55, 59-62 and 64-65 have been cancelled.

Status of Claims

Claims 3-6, 15, 58 and 63 are pending and under examination.

Claims 1-2, 7-14, 16-57, 59-62 and 64-65 have been cancelled.

Specification

The abstract of the disclosure is objected to because it uses the PCT abstract. Correction is required. See MPEP § 608.01(b).

Appropriate correction is required.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicants' cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6, 15, 58 and 63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written

description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification provides the definition for each of the component employed in the method. For example, "nucleic acid sequence", "polynucleotide sequence" or "polynucleotide" is defined as a nucleic acid (which is a polymer of nucleotides (A,C,T,U,G, etc.) or naturally occurring or representing a nucleic acid, depending on context. Either the given nucleic acid sequence or the complementary nucleic acid sequence can be determined from any specified polynucleotide sequence. Similarly, an "amino acid sequence" is defined as a polymer of amino acids (a protein, polypeptide, etc.) or a character string representing an amino

acid polymer, depending on context. The "population of cells" in the context of the present invention may be any population of any type of cell, in particular eukaryotic cells. The population may comprise cells expressing a library of polypeptides, e.g. a naive antibody library or a library of polypeptide variants where the aim is to identify antibodies or polypeptide variants in the library having a desired binding affinity, or it may comprise a collection of cell clones where the aim is to e.g. identify clones having a high and uniform expression level of a polypeptide of interest. For cell populations that express a library of polypeptides, these may for example be a naive antibody library, an antibody library obtained via immunization with a target of interest, or a library of an antibody or non-antibody polypeptide of interest. (Specification e.g., page 10, line 4 up to page 22, line 10). The definitions envision huge compounds of the method. The specification envisions at e.g., pages 45-47; a method of screening and selecting mammalian cell for monoclonal antibody (mab) for FACS-based enrichment. A full-length human antibody library is constructed. Two independent retroviral vectors exhibiting different antibiotic resistance markers are constructed to produce the mAB light chain library (LC lib) and heavy chain library (HC lib), as shown in Figures 19 and 20. As gleaned from the above description, the disclosure

describes only mab library in a retroviral vector with the stop codon that binds to antigen. Therefore, the skilled artisan cannot envision all the contemplated substance possibilities recited in the instant claim method as defined by the immense compounds provided in the definitions above. Even if one accepts that the example described in the specification meets the claim limitations of the rejected claims with regard to structure and function, the example is only representative of a single encoded polypeptide, mab that binds specifically to an antigen using retroviral. The results are not necessarily predictive of other cells, polypeptide variants, reporter peptide and termination suppression agent use in the method. Firstly, because the stop codons are not necessarily universal, with consideration variation amongst organelles (e.g., mitochondria and chloroplasts), viruses (e.g., single strand viruses), and protozoa (e.g., ciliated protozoa) as to whether the codons UAG, UAA, and UGA signal translation termination or encode amino acids. Even though a single release factor most probably recognizes all of the stop codons in eukaryotes, it appears that all of the stop codons are not suppressed in a similar matter. For example, in the yeast Saccharomyces pombe, nonsense suppression has to be strictly codon specific. In another example, significant differences were found in the degree of

suppression amongst three UAG codons and two UAA codons in different mRNA contexts in Escherichia coli and in human 293 cells, although data suggested that the context effects of nonsense suppression operated differently in E. coli and human cells. Since unconventional base interactions and/or codon context effects have been implicated in nonsense suppression, it is conceivable that compounds involved in nonsense suppression of one stop codon may not necessarily be involved in nonsense suppression of another stop codon. In other words, compounds involved in suppressing UAG codons may not necessarily be involved in suppressing UGA codons. (Welch et al, USP 72914610). Given the very large genus of cells, polypeptide variants, stop codons and termination suppression agent encompassed by the method claims, and given the limited description provided by the prior art and specification with regard to the regulation of stop codon read-through sequences that provide structures to support detectable binding, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus. There is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision the various claim components that satisfy the functional limitations

of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention.

Adequate written description requires more than a mere statement that it is part of the invention. See Fiefs v. Revel, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.II2, ¶1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6, 15, 58 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 3, step b) recites the limitation "the presence of a termination suppression agent." There is insufficient antecedent basis for this limitation in the claim.

2. This rejection has the same import to claim 6 "the surface of said cell".

3. Claim 15 recites the limitation "the absence of a termination suppression agent." There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more

than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 3, 6 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Light et al (U.S. Patent 5,770,356).

For claims 3, 6 and 15; Light discloses throughout the patent e.g., at col. 17, lines 30 up to col. 38, line 35 a method of expressing both anchored and non-anchored soluble heterologous polypeptides in a single vector in which nucleotide sequences are present for encoding: a) a suppressor tRNA gene capable of expressing a suppressor tRNA molecule; and b) an expression cassette for expressing a first and second heterologous polypeptide subunit. The cassette is designed to produce both subunits, one anchored to a phage membrane coat protein and the other not anchored, i.e., soluble, through the regulation of a nonsense chain termination codon and a tRNA suppressor gene. Exemplary expression cassettes for use with a

tRNA suppressor gene are present in expression vectors, the latter of which are those that provide for the expression of bacterial alkaline in either the non-anchored soluble form such as pPhoC as described in Example 8, or in the anchored form such as pPho8, pPhoL8 and pPhoL8B as described in Example 5. Light discloses the epitope tag at e., col. 39, line 65.

The broad claim method having undefined structures or features for the broad components is fully met by the method of Light.

Claims 3, 6 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Ciceri et al (USP 20070105093).

Ciceri et al discloses at e.g., the following claims; claim 1, a method of producing a fusion protein displayed on the surface of a phage in an expression system comprising a phage-derived nucleic acid construct containing a sequence encoding said fusion protein, said construct comprising, in a 5' to 3' orientation, a promoter and/or regulatory region operably linked to a sequence encoding a fusion protein further comprising a phage surface protein operably linked to a sequence comprising a termination codon operably linked to a sequence encoding a heterologous polypeptide; and a suppressor construct comprising,

in a 5' to 3' orientation, an inducible promoter and/or regulatory region operably linked to a sequence encoding a suppressor tRNA capable of recognizing said termination codon of said phage-derived nucleic acid construct; wherein said method comprises the steps of: (i) expressing the phage surface protein at the phage propagation step by not inducing said suppressor tRNA and (ii) expressing the phage-displayed fusion protein at the phage display step by inducing the expression of said suppressor tRNA.

2. The method of claim 1 wherein said expression system is in an E. coli cell.

14. The method of claim 1 wherein said suppressor tRNA is tRNA.sup.Ala or tRNA.sup.Glu.

15. The method of claim 1 wherein said suppressor tRNA is tRNA.sup.Ala.

16. A method of producing a fusion protein displayed on the surface of a phage comprising the steps of: (i) propagating said phage in a first expression system wherein said phage is a nucleic acid construct containing a sequence encoding said fusion protein, said construct comprising, in a 5' to 3' orientation, a promoter and/or regulatory region operably linked to a sequence encoding a fusion protein further comprising phage surface protein operably linked to a sequence comprising a termination codon operably linked to a sequence encoding a heterologous polypeptide; and (ii) expressing said fusion protein by inducing the expression of suppressor tRNA in a second expression system comprising said nucleic acid construct in step (i) and a suppressor construct comprising, in a 5' to 3' orientation, an inducible promoter and/or regulatory region operably linked to a sequence encoding said suppressor tRNA capable of recognizing said termination codon of said nucleic acid construct.

17. The method of claim 16 wherein said first expression system further comprises a second construct comprising, in a 5' to 3' orientation, an inducible promoter operably linked to a sequence encoding a phage surface protein, wherein expression of said phage surface protein aids the propagation of said phage.

18. The method of claim 18 wherein said expression system is in an E. coli cell.

Ciceri at e.g., paragraph [0038] discloses the phage derived and suppressor constructs of the invention are preferably selectable based upon different markers present on each construct.

Ciceri et al therefore anticipates the broad claim method using broad components.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-6, 15, 58 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ciceri or Light in view

Manuvakhova et al (RNA, 1000, 1044-55) and Sabbadini et al (7183105) and Nolan (WO 97/27212).

Each of Ciceri and Light is discussed above. Each of these references does not teach the suppressor agent as aminoglycoside antibiotic, the cells are screened by FACS machine and the cell membrane is GPI as the cell membrane anchoring peptide. However, Manuvakhova et al teaches at e.g., page 1044, the abstract that aminoglycoside antibiotics can reduce the efficiency of translation termination. Manuvakhova further teaches at page 1045, col. 2 that G418 can suppress premature stop mutations in a gene. Sabbadini disclose at e.g., col. 127, line 29 up to col. 128, line 5, FACS analysis of isolated cells. Sabbadini further discloses at e.g., col. 165, lines 26-50 the incorporation of GPI anchors and other membrane-targeting elements into the amino-or carboxy-terminus of a fusion protein can direct the chimeric molecule to the cell surface. Nolan teaches that phenotypic changes of cells that can be sorted out using FACS. Note e.g., page 3, lines 6-13; page 4, lines 26-27. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use FACS to screen cells as this is the conventional way of screening or sorting out cells from a pool or library as taught by Nolan or Sabbadini. One would have a reasonable expectation of success

since FACS has been used to screen cells in a population as achieved by Sabbadini or Nolan. Furthermore to use aminoglycoside antibiotic as the suppressor agent as taught by Manuvakhova in the method of Light or Cicero would be expected since amino glycoside has been tested for different cells and found to suppress termination cordons. Likewise, it would have been obvious to use GPI in the method of Light or Cicero as taught by Sabatini reasonably expecting that since GPI is a known membrane anchoring peptide would provide the anchor for the peptide to the cells. Accordingly, the combined teachings of the prior art renders the claim prima facie obvious to one having ordinary skill in the art at the time of filing.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the

organization where this application or proceeding is assigned is

571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639